Blood culture PCR Interpretation Education

The Antimicrobial Stewardship Team endorses the use of blood culture PCR to aid in clinical decision making regarding selecting appropriate empiric anti-infective therapy when used in context with clinical judgement. PCR results are considered highly accurate, and studies show improved time to effective therapy without adverse effects on mortality. Final results of antimicrobial susceptibility testing should be used to further guide definitive therapy. This only applies to blood cultures and empiric therapy. Refer also to the antibiogram for additional information.

This document is meant to be general and educational. Antibiotic selection should take into account source of infection, severity, and patient specific factors. If there are questions about a specific case, please feel free to contact the AMS pharmacist to review or consult ID as needed.

Gram Positive Bacteria

Pathogen Detected	Preferred Therapy	Comments
Enterococcus faecalis	Ampicillin	
Enterococcus faecium	VanA/B not detected = Vancomycin VanA/B detected = Daptomycin	Recommend ID consult
Listeria monocytogenes	Ampicillin	
Staphylococcus spp. (no species identified)	Likely CoNS, probable contaminant	Can consider withholding treatment if clinically stable and no suspected source of infection. Repeat blood cultures may be helpful.
Staphylococcus spp *Staphylococcus aureus*	mecA/C and MREJ - Cefazolin or nafcillin mecA/C and MREJ + vancomycin Note: A combined molecular detection of *mecA/C,* MREJ, and *S. aureus* indicates MRSA.	Automatic ID consult for *S aureus* bacteremia
Staphylococcus spp. *Staphylococcus epidermidis*	Probable contaminant	Can consider withholding treatment if clinically stable and no suspected source of infection. Repeat blood cultures may be helpful.
Staphylococcus spp. *Staphylococcus lugdunensis*	mecA/C - Cefazolin or nafcillin mecA/C + vancomycin	Generally treated similarly to *S aureus.*
Streptococcus spp. (no species identified)	Ceftriaxone	May represent contamination if low growth and certain speciation (i.e., ¼ bottles *S viridans*) without source of infection. Requires interpretation.
Streptococcus spp. *Streptococcus agalactiae*	Ceftriaxone	
Streptococcus spp. *Streptococcus pneumoniae*	Ceftriaxone	
Streptococcus spp. *Streptococcus pyogenes*	Ceftriaxone or ampicillin/sulbactam	

Gram Negative Bacteria

Pathogen Detected	Preferred Therapy	Comments
Acinetobacter calcoaceticusbaumannii complex	Cefepime	
Bacteroides fragilis	Metronidazole or Piperacillin/tazobactam	
Enterobacterales *Enterobacter cloacae complex*	Cefepime	Also evaluate resistance genes and alter therapy accordingly. If source of infection is suspected to be polymicrobial remember to consider anaerobic coverage if appropriate. Severity of infection, immune status, patient factors may all impact selection. *Examples: 1) For a neutropenic patient with E.coli bacteremia cefepime may be more appropriate than ceftriaxone. 2) An intraabdominal infection with E.coli may require piperacillin/tazobactam or ceftriaxone + metronidazole. 3) For ESBL + E.coli, consider ertapenem empirically. 4) A stable patient with community onset urosepsis and E.coli bacteremia without resistance, ceftriaxone is reasonable empirically.*
Enterobacterales *Escherichia coli*	Ceftriaxone	
Enterobacterales *Klebsiella aerogenes*	Cefepime	
Enterobacterales *Klebsiella oxytoca*	Ceftriaxone	
Enterobacterales *Klebsiella pneumoniae group*	Ceftriaxone	
Enterobacterales *Proteus spp.*	Ceftriaxone	
Enterobacterales *Salmonella spp.*	Ceftriaxone	
Enterobacterales *Serratia marcescens*	Cefepime	
Haemophilus influenzae	Ceftriaxone	
Neisseria meningitidis	Ceftriaxone	
Pseudomonas aeruginosa	Ceftazidime, cefepime, or piperacillin/tazobactam	
Stenotrophomonas maltophilia	TMP/SMX	

Resistance Genes	Comments
Carbapenemases IMP KPC OXA-48-like NDM VIM	Isolation precautions for MDROs Consider ID consult
Colistin Resistance *mcr-1*	Isolation precautions for MDROs Consider ID consult
ESBL CTX-M	Isolation precautions for MDROs Consider empiric carbapenem therapy Enterobacterales + ESBL: generally, ertapenem is appropriate empirically
Methicillin Resistance *mecA/C* *mecA/C* and MREJ (MRSA)	Evaluate associated species Generally, vancomycin is appropriate empirically Note: *mecA/C,* MREJ combined is associated *S. aureus* Note: *mecA/C alone is associated with Staphylococcus species not aureus.*
Vancomycin Resistance *vanA/B*	Daptomycin Consider ID consult

Yeast	Preferred Therapy	Comments
Candida albicans	Micafungin	Generally, an echinocandin (micafungin) is the preferred empiric therapy for Candidemia. Alternatives and step-down therapy may vary depending on isolate, susceptibility, and infection source. ID consult is recommended.
Candida glabrata	Micafungin	
Candida krusei	Micafungin	
Candida parapsilosis	Fluconazole	
Candida tropicalis	Micafungin	
Candida auris	ID consult	+ Isolation
Cryptococcus (C. neoformans/C. gattii)	ID consult	

FAQs:

- This PCR shows "Enterobacterales" and "E.coli" is this a polymicrobial culture?
  - No: Bacterial taxonomy has been updated. What we used to refer to as the Family *Enterobacteriaceae* is now considered multiple Families so this group of bacteria is generally referred to now as the Order *Enterobacterales*, of which *E. coli*, *Klebsiella spp*, and others are members. So, the presence of both *Enterobacterales* and *E.coli* just means there is *E.coli* present.

- The PCR is positive for a MEC / Methicillin Resistance gene does this mean it is MRSA?
  - Not necessarily. Mec genes can be associated with other non-aureus Staph species such as *S. epidermidis* which often represents contamination. Look for which species was also identified. MREJ + is specifically MRSA (CoNS do not have this one). For example: a combined molecular detection of *mecA/C,* MREJ, and *S. aureus* indicates MRSA.

- The PCR shows MSSA should I wait until the blood culture is final to narrow to cefazolin or nafcillin?
  - The AMS team endorses optimizing therapy for MSSA with an antistaphylococcal beta-lactam based on blood culture PCR instead of waiting on final results if consistent with the clinical scenario.

- A Gram positive was identified but the PCR was negative / did not identify a species???
  - Some common skin contaminants such as diphtheroid, *Micrococcus*, and *Bacillus spp* are not identified by PCR Panel. Some other bacteria such as *Corynebactrium* and some anaerobes are also not specifically identified by the PCR panel and must be interpreted in the clinical context.

- PCR shows yeast is this a contaminant?
  - No. Yeast on a blood culture should be interpreted as significant and treated.

References:

1. Biofire Blood culture Identification 2 (BCID2) Panel product information. https://www.biomerieux-diagnostics.com/biofire-filmarray-bcid2-panel

    - **Accurate**: The average positive agreement rate (or sensitivity) across all pathogens on the BCID2 panel is 99%, and the negative agreement rate (or specificity) is 99.8%[1]

2. Liaquat S,l Baccaglini L, Haynatzki G, et al. Clinical consequences of contaminated blood cultures in adult hospitalized patients at an institution utilizing a rapid blood-culture identification system. *Infect Control Hosp epidemiol.* 2021;42(8):978-84. https://pubmed.ncbi.nlm.nih.gov/33298207/
    - Despite the use of molecular-based, rapid blood-culture identification, contamination of blood cultures continues to result in prolonged hospital stay and unnecessary antibiotic therapy in hospitalized patients.
3. MacVane SH, Note FS. Benefits of Adding a Rapid PCR-Based Blood Culture Identification Panel to an Established Antimicrobial Stewardship Program. *J Clin Microbiolo* 2016;54(10):2455-2463. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5035429/
    - No difference between the control group, AS group, and BCID group was seen with respect to mortality, 30-day readmission, intensive care unit length of stay (LOS), postculture LOS, or costs. In patients with BSI, ASP alone improved antimicrobial utilization. Addition of BCID to an established ASP shortened the time to effective therapy and further improved antimicrobial use compared to ASP alone, even in a setting of low antimicrobial resistance rates.
4. Britt NS, Khader K, He T, et al. Examining the clinical impact of rapid multiplex polymerase chain reaction-based diagnostic testing for bloodstream infections in a national cohort of the Veterans Health Administration. *Pharamcotherapy* 2023;43(1):24-34. https://pubmed.ncbi.nlm.nih.gov/36484553/
    - Statistically significant improvement in early appropriate therapy within 48 hours in the post PCR group. No difference in 30-day mortality.
5. Adeolu M, Alnajar S, Naushad S, Gupta RS. Genome-based phylogeny and taxonomy of the 'Enterobacteriales': proposal for Enterobacterales ord. nov. divided into the families Enterobacteriaceae, Erwiniaceae fam. nov., Pectobacteriaceae fam. nov., Yersiniaceae fam. nov., Hafniaceae fam. nov., Morganellaceae fam. nov., and Budviciaceae fam. nov. *Int J Syst Evol Microbiol* 2016;66:5575–5599. https://www.microbiologyresearch.org/content/journal/ijsem/10.1099/ijsem.0.001485
6. AJ McAdam. Enterobacteriaceae? Enterobacterales? What Should We Call Enteric Gram-Negative Bacilli? A Micro-Comic Strip. *J Clin Micro.* 1/28/2020 https://journals.asm.org/doi/10.1128/jcm.01888-19

Puget Sound Region (St Peter and Centralia Hospitals) AMS team. 2023